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Cutaneous Sarcoidosis in a Patient With Philadelphia-Positive Chronic Myelogenous Leukemia Treated With Interferon-α

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A patient with Philadelphia-positive (Ph+) chronic myelogenous leukemia (CML) was diagnosed with cutaneous sarcoidosis after treatment with interferon-alpha (IFN-α). Following IFN-α dose reduction, the skin lesions disappeared. Few cases of sarcoidosis associated with IFN treatment have been reported, and only in one patient with preexisting CML. Our patient was unique in that (1) the sarcoidosis was induced by the IFN-α treatment alone, (2) it developed de novo, and (3) it was confined to the skin. Am. J. Hematol. 58:80–81, 1998. © 1998 Wiley-Liss, Inc.

Key words: interferon-α; sarcoidosis; chronic myelogenous leukemia; monocytosis

INTRODUCTION

Sarcoidosis is a multi-system granulomatous disorder and the pathogenesis is thought to be an exaggerated immune response to unknown antigens. T lymphocytes and mononuclear cells form non-caseating granulomas. Cytokine production by sarcoid tissue, including IL-2, TNF-alpha, and IFN-gamma has been described (reviewed in [1]). We report a case of cutaneous sarcoidosis related to IFN-α therapy in a CML patient.

CASE REPORT

A 48-year-old female presented in April 1994 with an elevated white blood cell (WBC) count. The only physical examination abnormality was a palpable spleen tip. Initial laboratories: Peripheral blood (PB): Hb 9.7 g/dl, WBC 38,700/μl, with 63% neutrophils, 17% bands, 7% lymphocytes, 2% monocytes, 4% metamyelocytes, and 7% myelocytes. Platelet count was 366,000/μl. Bone marrow (BM) was hypercellular (M:E ratio of 11:1), with normal maturation except for an increased number of myelocytes with monocytoid features. Twenty of 20 BM metaphases contained the Philadelphia chromosome; t(9;22)(q34;q11.2). Chest X-ray was unremarkable.

The patient was started on hydroxyurea. In June 1994, the WBC increased to 66,700/μl with a PB monocytosis of 2,300/μl. In July 1994, IFN-α was substituted for hydroxyurea at 3 million units (MU)/m^2 subcutaneous injection (6 MU) daily, increasing to 9 MU daily. The WBC count dropped to 5,500/μl over 3 months, with PB differential of 43% neutrophils, 12% bands, 25% lymphocytes, 14% monocytes, 6% metamyelocytes. BM biopsy was 100% cellular, with 6 of 20 normal metaphases. In February 1995, IFN-α was decreased to 6 MU daily, due to thrombocytopenia. Eleven of 20 BM metaphases were normal.

In March 1995, non-pruritic papules developed on both eyelids and forearms. The papules worsened and multiple 1–3-cm subcutaneous nodules appeared on the arms, legs, and trunk, associated with fatigue. The IFN-α was decreased to 5 MU a day, with fatigue resolution but persistent nodules. Skin biopsy in May 1995 showed non-caseating epithelioid granulomas in the reticular dermis and adipose tissue, consistent with sarcoidosis. Fungal and acid-fast stains along with skin cultures were negative. Chest X-ray and eye examination were normal. Fifteen of 21 BM metaphases were normal (June 1995). IFN-α was decreased to 4 MU daily and the skin lesions

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regressed. In August 1995, WBC count was 4,520/μl with a normal differential. BM cellularity was 50% with an M:E ratio of 3:1. One of 13 BM metaphases was Ph+ positive. The sarcoid lesions continued to regress and were gone by February 1996. The patient was maintained on 4 MU IFN-α daily.

DISCUSSION

There are 4 reported cases of sarcoidosis with CML. Three patients had underlying sarcoidosis when diagnosed with CML [2–4]. In the fourth, both diseases were diagnosed simultaneously [5]. The incidence of both diseases is low, and they may have occurred together spontaneously.

A variety of complications of IFN-α therapy have been reported [6], but there have been only 3 sarcoidosis cases [4,7,8]. IFN-α and IFN-γ therapy exacerbated preexisting sarcoidosis in one CML patient [4]. Another hepatitis C patient developed cutaneous sarcoidosis during IFN-α treatment [8]. Of interest is a recent observation that dermal infiltration of CD4-positive T lymphocytes occurs in skin eruptions caused by IFN-α [9]. Activation of CD4-positive T lymphocytes initiates granuloma formation.

Other factors may account for this combination of CML and sarcoidosis. Otherwise a typical CML, our case possessed distinct features including: no basophilia, a PB monocytosis, and myelocytes with monocytic characteristics in the BM. These features are consistent with Ph+ chronic myelomonocytic leukemia, proposed in 1986 [10]. We postulate that these ''myelomonocytes'' could have promoted granuloma formation.

In conclusion, we report a case of cutaneous sarcoidosis that developed during IFN-α therapy for CML. We believe that IFN-α, acting as an immunomodulator with the monocytic component of the CML, was involved in the pathogenesis of this unusual combination of diseases. This is supported by the sarcoidosis regression after decreasing the IFN-α dose.

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